



PATENT  
Docket No. 300622000123

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In the application of:

Chaitan KHOSLA et al.

Serial No.: 09/925,236

Filing Date: August 8, 2001

For: RECOMBINANT PRODUCTION OF  
NOVEL POLYKETIDES

Examiner: To Be Assigned

Group Art Unit: 1652

**INFORMATION DISCLOSURE  
STATEMENT UNDER 37 C.F.R. § 1.97**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

Pursuant to 37 C.F.R. § 1.97 and § 1.98, Applicants submit for consideration in the above-identified application the documents listed on the attached Form PTO-1449. Copies of the documents were previously submitted in an Information Disclosure Statement and/or Office Action, directed to the related application Serial Number 09/263,184, filed March 5, 1999, and, accordingly, copies are not included herewith. This protocol conforms with 37 C.F.R. § 1.98(d) and M.P.E.P. 609(A)(2). The Examiner is requested to make these documents of record in the application.

This application is a continuation of U.S. Patent Application Serial No. 09/263,184, filed March 5, 1999, which is a divisional of U.S. Patent Application Serial No. 08/828,898, filed March 31, 1997, now U.S. Patent No. 6,022,731, which is a continuation of U.S. Patent Application Serial No. 08/238,811, filed May 6, 1994, now U.S. Patent No. 5,672,491, which is a continuation-in-part of U.S. Patent Application Serial No. 08/164,301, filed December 8, 1993, which is a continuation-in-part of U.S. Application Serial No. 08/123,732, filed September 20, 1993, from which priority is claimed pursuant to 35 U.S.C. §120.

This Information Disclosure Statement is submitted:

- ☐ With the application; accordingly, no fee or separate requirements are required.
- ☒ Within three months of the application filing date or before mailing of a first Office Action on the merits; accordingly, no fee or separate requirements are required.
- ☐ After receipt of a first Office Action on the merits but before mailing of a final Office Action or Notice of Allowance.
  - ☐ A fee is required. A check in the amount of \* is enclosed.
  - ☐ A fee is required. Accordingly, a Fee Transmittal form (PTO/SB/17) is attached to this submission in duplicate.
  - ☐ A Certification under 37 C.F.R. § 1.97(e) is provided below; accordingly, no fee is believed to be due.
- ☐ After mailing of a final Office Action or Notice of Allowance, but before payment of the issue fee.
  - ☐ A Certification under 37 C.F.R. § 1.97(e) is provided below and a check in the amount of \* is enclosed.
  - ☐ A Certification under 37 C.F.R. § 1.97(e) is provided below and a Fee Transmittal form (PTO/SB/17) is attached to this submission in duplicate.

Applicants would appreciate the Examiner initialing and returning the Form PTO-1449, indicating that the information has been considered and made of record herein.

The information contained in this Information Disclosure Statement under 37 C.F.R. § 1.97 is not to be construed as a representation that: (i) a complete search has been made; (ii) additional information material to the examination of this application does not exist; (iii) the information, protocols, results and the like reported by third parties are accurate or enabling; or (iv) the above information constitutes prior art to the subject invention.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing 300622000123. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: November 25, 2002

Respectfully submitted,

By: Brenda J. Wallach  
Brenda J. Wallach  
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Form PTO-1449

# INFORMATION DISCLOSURE CITATION IN AN APPLICATION

(Use several sheets if necessary)

Docket Number 300622000123

Application Number 09 925,236

Applicant

Charan KHOSLA et al

Filing Date August 8, 2001

Group Art Unit 1652

Mailing Date November 25, 2002

## U.S. PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Name	Class	Subclass	Filing Date If Appropriate
	1.	06/1990	4,935,340	Baltz <i>et al.</i>			
	2.	09/1997	5,672,491	Khosla <i>et al.</i>			
	3.	10/1998	5,824,513	Katz <i>et al.</i>			
	4.	11/1998	5,830,750	Khosla <i>et al.</i>			
	5.	10/1999	5,962,290	Khosla <i>et al.</i>			
	6.	12/1999	6,004,787	Katz <i>et al.</i>			
	7.	02/2000	6,022,731	Khosla <i>et al.</i>			
	8.	05/2000	6,060,234	Katz <i>et al.</i>			
	9.	05/2000	6,063,561	Katz <i>et al.</i>			
	10.	03/2001	6,200,813	Katz <i>et al.</i>			
	11.	08/2001	6,271,255	Leadlay <i>et al.</i>			

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## FOREIGN PATENT DOCUMENTS

Examiner Initials	Ref. No.	Date	Document No.	Country	Class	Subclass	Translation YES NO
	12.	10/1983	EP 0092388	Europe			
	13.	17.01.92	WO 93/13663	PCT			

## OTHER DOCUMENTS

(including author, title, Date, Pertinent Pages, Etc.)

Examiner Initials	Ref. No.	Title
	14.	Bartel, <i>et al.</i> , "Biosynthesis of anthraquinones by interspecies cloning of actinorhodin biosynthesis genes in streptomycetes: Clarification of actinorhodin gene functions," <i>J Bacteriol</i> (1990) 172(9):4816-4826
	15.	Beck, <i>et al.</i> , "The multifunctional 6-methylsalicylic acid synthase gene of <i>Penicillium patulum</i> . Its gene structure relative to that of other polyketide synthases," <i>Eur J Biochem</i> (1990) 192:487-498
	16.	Bibb, <i>et al.</i> , "Analysis of the nucleotide sequence of the <i>Streptomyces glaucescens</i> tcmI genes provides key information about the enzymology of polyketide antibiotic biosynthesis." <i>EMBO J</i> (1989) 8(9):2727-2735

EXAMINER:

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INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION

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Docket Number 300622000123

Application Number 09 925,236

Applicant

Chaitan KHOSLA et al.

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Group Art Unit 1652

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## OTHER DOCUMENTS

(including author, title, Date, Pertinent Pages, Etc.)

Examiner Initials	Ref. No.	Title
	17.	Caballero <i>et al.</i> , "Organisation and functions of the actVA region of the actinorhodin biosynthetic gene cluster of <i>Streptomyces coelicolor</i> ," <i>Mol Gen Genet</i> (1991) 230:401-412
	18.	Cortes <i>et al.</i> , "n unusually large multifunctional polypeptide in the erythromycin-producing polyketide synthase of <i>Saccharopolyspora erythraea</i> ," <i>Nature</i> (1990) 348:176-178
	19.	Davis, <i>et al.</i> , "Functional mapping of a polyketide synthase from <i>Aspergillus terreus</i> involved in lovastatin synthesis," <i>Abst of the Genetics of Industrial Microorganisms Mtg</i> (1994) P288:192
	20.	Donadio <i>et al.</i> , "Modular organization of genes required for complex polyketide biosynthesis," <i>Science</i> (1991) 252:675-679
	21.	Donadio <i>et al.</i> , "Biosynthesis of the erythromycin macrolactone and a rational approach for producing hybrid macrolides," <i>Gene</i> (1992) 115:97-103
	22.	Fernandez-Moreno <i>et al.</i> , "the act cluster contains regulatory and antibiotic export genes, direct targets for translational control by the bldA tRNA gene of <i>Streptomyces</i> ," <i>Cell</i> (1991) 66:769-780
	23.	Fernandez-Moreno <i>et al.</i> , "Nucleotide sequence and deduced functions of a set of cotranscribed genes of <i>Streptomyces coelicolor</i> A3(2) including the polyketide synthase for the antibiotic actinorhodin," <i>J Biol Chem</i> (1992) 267:19278-19290
	24.	Floss, "Genetic engineering of hybrid antibiotics - a progress report," <i>Tetrahedron</i> (1991) 47(31):6045-6058
	25.	Fu, "Engineered biosynthesis of novel polyketides: Stereochemical course of two reactions catalyzed by a polyketide synthase," <i>Biochemistry</i> (1994) 33(31):9321-9326
	26.	Hallam, "Nucleotide sequence, transcription and deduced function of a gene involved in polyketide antibiotic synthesis in <i>Streptomyces coelicolor</i> ," <i>Gene</i> (1988) 74:305-320
	27.	Hershberger <i>et al.</i> , "Genetics and molecular biology of industrial microorganisms," <i>Am Soc for Microbiol</i> (1989) (Washington, D.C.) pages 68-84
	28.	Hopwood <i>et al.</i> , "Antibiotics: opportunities for genetic manipulation," <i>Phil Trans R Soc Lond</i> (1989) B324:549-562
	29.	Hopwood <i>et al.</i> , "Product of 'hybrid' antibiotics by genetic engineering," <i>Nature</i> (1985) 314 (6012):642-644
	30.	Hutchinson, "Drug synthesis by genetically engineered microorganisms," <i>Ann Review Microbiol</i> (1993) 47:875-912
	31.	Katz <i>et al.</i> , "Polyketide synthesis: Prospects for hybrid antibiotics," <i>Ann. Review Microbiol</i> (1993) 47:875-912

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INFORMATION DISCLOSURE CITATION  
IN AN APPLICATION

(Use several sheets if necessary)

Docket Number 300622000123

Application Number 09 925 296

Applicant

Chaitan KHOSLA et al.

Filing Date August 8, 2001

Group Art Unit 1652

Mailing Date November 25, 2002

## OTHER DOCUMENTS

(including author, title, Date, Pertinent Pages, Etc.)

Examiner Initials	Ref. No.	Title
	32.	Khosla, <i>et al.</i> , "Targeted gene replacements in a <i>Streptomyces</i> polyketide synthase gene cluster: role for the acyl carrier protein," <i>Mole Microbiol</i> (1992) 6(21):3237-3249
	33.	Khosla, <i>et al.</i> , "Genetic construction and functional analysis of hybrid polyketide synthases containing heterologous acyl carrier proteins," <i>J Bacteriol</i> (1993) 175:2197-2204
	34.	MacNeil <i>et al.</i> , "Complex organization of the <i>Streptomyces avermitilis</i> genes encoding the avermectin polyketide synthase," <i>Gene</i> (1992) 115:119-125
	35.	Malpartida <i>et al.</i> , "Molecular cloning of the whole biosynthetic pathway of a <i>Streptomyces</i> antibiotic and its expression in a heterologous host," <i>Nature</i> (1984) 309:462-464
	36.	Malpartida <i>et al.</i> , "Physical and genetic characterisation of the gene cluster for the antibiotic actinorhodin in <i>Streptomyces coelicolor</i> A3(2)," <i>Mol Gen Genet</i> (1986) 205:66-73
	37.	Malpartida <i>et al.</i> , "Homology between <i>Streptomyces</i> genes coding for synthesis of different polyketides used to clone antibiotic biosynthetic genes," <i>Nature</i> (1987) 325(6107):818-821
	38.	McDaniel <i>et al.</i> , "Engineered biosynthesis of novel polyketides," <i>Science</i> (1993) 262:1546-1550
	39.	Roberts, <i>et al.</i> , "6-Deoxyerythronolide B synthase 3 from <i>Saccaropolyspora erythraea</i> : Over-expression in <i>Escherichia coli</i> , purification and characterisation," <i>Biochem Soc Trans</i> (1992) 21:325
	40.	Roberts, <i>et al.</i> , "Heterologous expression in <i>Escherichia coli</i> of an intact multienzyme component of the erythromycin-producing polyketide synthase," <i>Eur J Biochem</i> (1993) 214:305-311
	41.	Robinson, "Polyketide synthase complexes: their structure and function in antibiotic biosynthesis," <i>Phil Trans R Soc Land B</i> (1991) 332:107-114
	42.	Rohr, "Combinatorial biosynthesis - an approach in the near future?" <i>Angew Chem Int Ed Engl</i> (1995) 34(8):881-885
	43.	Sherman <i>et al.</i> , "Structure and deduced function of the granaticin-producing polyketide synthase gene cluster of <i>Streptomyces violaceoruber</i> Tü22," <i>EMBO J</i> (1989) 8:2717-2725
	44.	Sherman <i>et al.</i> , "Functional replacement of genes for individual polyketide synthase components in <i>Streptomyces coelicolor</i> A3(2) by heterogenous genes from a different polyketide pathway," <i>J Bacteriol</i> (1992) 174:6184-6190
	45.	Strohl, <i>et al.</i> , "Expression of polyketide biosynthesis and regulatory genes in heterologous streptomycetes," <i>J Ind Microbiol</i> (1991) 7:163-174
	46.	Strohl <i>et al.</i> , "Significance of anthraquinone formation resulting from the cloning of actinorhodin genes in heterologous streptomycetes," <i>Molecular Microbiology</i> (1992) 6(2):147-152
	47.	Tsoi, <i>et al.</i> , "Combinatorial biosynthesis of unnatural and natural products: the polyketide example." Database Caplus on STN. Chemical Abstract No. 123:169385

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Form PTO-1449  INFORMATION DISCLOSURE CITATION IN AN APPLICATION  (Use several sheets if necessary)	Docket Number 300622000123	Application Number 09 925,236
	Applicant  Charan KHOSLA et al.	
	Filing Date August 8, 2001	Group Art Unit 1652
	Mailing Date November 25, 2002	

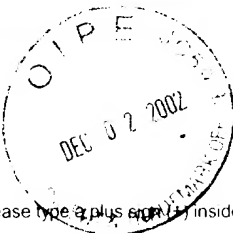
OTHER DOCUMENTS

(including author, title, Date, Pertinent Pages, Etc.)

Examiner Initials	Ref. No.	Title
	48.	Tuan <i>et al.</i> , "Cloning of Genes Involved in Erythromycin biosynthesis from <i>Saccharopolyspora erythrae</i> using a novel actinomycete- <i>Escherichia coli</i> cosmid," <i>Gene</i> (1990) 90:21-29
	49.	Tsoi, <i>et al.</i> , "Combinatorial biosynthesis of unnatural and natural products: the polyketide example," <i>Chem. Biol.</i> , 2(6):355-362

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<b>TRANSMITTAL FORM</b>  (to be used for all correspondence after initial filing)	<b>Application Number</b>	09/925,236	
	<b>Filing Date</b>	August 8, 2001	
	<b>First Named Inventor</b>	KHOSLA	
	<b>Group Art Unit</b>	1652	
	<b>Examiner Name</b>	To Be Assigned	
<b>Total Number Of Pages In This Submission</b>	8	<b>Attorney Docket No.</b>	300622000123

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<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53		

**SIGNATURE OF APPLICANT, ATTORNEY OR AGENT**

Firm or Individual Name	Brenda J. Wallach Registration No. 45,193
Signature	
Date	November 25, 2002

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Garee A. Haney

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